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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/587,714	06/04/2007	Jane K. Relton	2681.0450001	2306

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EXAMINER	
WEGERT, SANDRA L	

ART UNIT	PAPER NUMBER
1646	

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04/14/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/587,714	RELTON ET AL.	
	Examiner	Art Unit	
	SANDRA WEGERT	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 December 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,6,10-12 and 19-36* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4, 6, 10-12 and 19-36* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *28 July 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Detailed Action

The amendment and Remarks, submitted 22 December 2009, have been entered and considered. Claims 1-4, 6, 10-12 and 19-36 are pending. Claims 5, 7-9 and 13-18 have been cancelled. Claims 1-4, 6, 10 and 23 have been amended. Claims 24-36 are new.

Claims 1-4, 6, 10-12 and 19-36 are under examination in the Instant Application.

Withdrawn Claim Rejections/Objections

Typographic-

The objection to claim 15 for a typographic error is *withdrawn*. Applicants cancelled claim 15 (22 December 2009).

35 USC § 112, first paragraph – Written Description.

The rejection of claims 1-4, 6, 10-12 and 19-21, under 35 U.S.C. 112, first paragraph, for lack of written description, is *withdrawn*. This rejection was made in a previous Office action (24 September 2009, p. 7-8) because the claims recited or embraced "an NgR1 antagonist" or antibodies that bind a "polypeptide comprising SEQ ID NO: 3." Applicants amended pending claims to remove reference to "an NgR1 antagonist," and cancelled claim 17 (22 December 2009).

Maintained Claim Rejections/Objections

Claim Rejections - 35 USC § 112, first paragraph – Breadth.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> **The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.**

Claims 1-4, 6, 10-12 and 19-21 *remain* rejected under 35 USC 112, first paragraph, because the specification, while being enabling for a method of promoting regeneration or survival of dopaminergic neurons in mammals injected with the toxin 6OHDA, by administering soluble NgR1 intracranially, does not enable a method of promoting regeneration or survival of dopaminergic neurons in a mammal in which dopamine neurons died from a degenerative disease, or in which the sNgR1 receptor is not administered intracranially, or in which NgR antagonists other than sNgR1 are administered. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims. This rejection also applies to new claims 24-34.

Claims 1-4, 6, 10-12, 19-21 and 24-34 embrace all methods of promoting restoration of dopamine neurons after any injury in the brain involving dopamine neurons, including those involved in human diseases such as Parkinson's disease, and those using non-confirmed antagonists of NgR besides sNgR1 (as exemplified by claims 24-34). Experiments presented in the specification show that NOGO receptor (NgR) knockout mice display less apparent cell loss

when injected with 6OHDA (a toxin that specifically targets dopaminergic neurons throughout the brain). The inventors used conventional tests of dopaminergic cell number and function, such as tyrosine hydroxylase (TH) staining in the striatum (the enzyme used to produce dopamine), as well as movement studies in which the 6OHDA is injected into one side of the striatum only, and the rat's rotational bias toward the contralateral side is measured. However, the claims also embrace methods of treating all dopaminergic brain disorders, using any NgR1 antagonist, and by any means of administration. The claims also encompass methods of treating diseases that involve dopamine cell degeneration, including those that are not confirmed as involving the NgR1 receptor or any NOGO receptor.

In addition, the instant Application also does not reasonably provide enablement for use of variants of NgR1, such as amino acids 26-310 of SEQ ID NO: 3 *with up to ten conservative amino acid substitutions*, as recited in claim 6. Although amino acids 26-310 of SEQ ID NO: 3, the soluble form of NgR1, appears to act as an antagonist at NOGO receptors in the striatum (Figure 2B), no variants of sNgR1 were made or used in any of the experiments described, as pointed out in the previous office action (24 September 2009, pp. 4-5).

Applicants argue that the breadth rejection is incorrect and assert that any person skilled in the relevant art can make or use the invention without undue experimentation and cite In re Wands (858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed Cir. 1988)) and In re Wright (CAFC) 27 USPQ2d 1510 at 1513 (22 December 2009, p. 12). Applicant's arguments filed 22 December 2009 have been fully considered but they are not persuasive for the following reasons:

The first paragraph of 35 USC § 112 requires that the enabling specification must teach those skilled in the art how to make and use the claimed invention without undue

experimentation. Case law indeed confirms that the disclosure of a patent application must enable the invention: *"To be enabling, the specification of a patent must teach those skilled in the art how to make and use the full scope of the claimed invention without 'undue experimentation'."* (Wands', 858 F.2d at 736-37, 8 USPQ2d at 1404; In re Fisher, 427 F.2d 833,839, 166 USPQ 18, 24 (CCPA 1970)) and: *"the first paragraph of section 112 requires that the scope of protection sought in a claim bear a reasonable correlation to the scope of enablement provided by the specification"* (In re Wright (CAFC) 27 USPQ2d 1510 at 1513). Thus, the cited case law supports the examiner's position that the instant disclosure is not sufficient to enable the invention without "undue experimentation." For example, it is not known how experiments with NOGO-knockout mice could provide evidence to support a method of treatment of human beings with neurodegenerative diseases. The nexus between the knockout mice and a role for NOGO in Parkinson's disease and other neurodegenerative diseases is tenuous at best and would be made more clear if there were more experimentation that at least addressed that issue. In addition, while it is generally assumed that adding a soluble receptor will competitively bind ligands for the receptor, thus acting indirectly as an "antagonist," it is not at all clear-cut that *any* antibodies or antibody fragments would display the same function (referring to claims 24-34).

Applicants also argue that "an applicant is not limited to the confines of the specification" to enable an invention, and cite *Howarth (*654 F.2d at 105-6, 210 USPQ at 692) and *Genentech (Genentech v. Novo Nordisk,* 108 F.3d 1361, 1366, 42, USPQ2d 1001, 1005, Fed. Cir. 1997) (Remarks, p. 13). The examiner agrees that one need not supply information that is well known in the art. However, administration of a NOGO antagonist to treat any dopaminergic

neurodegenerative disease is not a well known (and thus enabled) process, and there is little evidence from the literature that NOGO is involved in the etiology of "dopaminergic neuronal degeneration" (claim 1), or responsible for such poor outcomes in neurodegenerative diseases when attempts are made at treatment. The examiner also agrees that the 6OHDA model of selective dopaminergic ablation is a valid experimental model that focuses on destruction only of dopaminergic cells. However, it is not a valid model that mimics all or many neurodegenerative diseases that would fall into the genus of those that would be covered by the claimed method.

As far as whether the claimed variants of sNgR1 are enabled, as described in claim 6, applicants assert that it would be routine in the art to simply make and test all or many of the variants claimed (Remarks, p. 17), and cite Barton, et al (2003, EMBO J., 22(13): 3291-3302, of record). The examiner agrees that it is routine in the art to mutate the coding sequence of any polypeptide to generate any variant possible (Remarks, p. 17, paragraph 2). However, it would require undue experimentation to make and test enough examples of polypeptides with up to ten amino acid substitutions, *even with* the guidance in comparative structure of NOGO receptors provided by Barton, et al. There is not enough experimental evidence that polypeptides with up to ten substitutions function **just like sNgR1**, such that the genus is enabled and the newly-made variants inhibit NOGO receptor-mediated activity with the same affinity and specificity as the one soluble receptor "antagonist" described in the specification.

Claim Rejections - 35 USC § 112, first paragraph – Lack of Enablement

Claims 22 and 23 *remain* rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. This rejection also applies to new claims 35 and 36.

The rejection was made previously (24 September 2009, p. 6) because the instant specification does not reasonably provide enablement for a method of promoting regeneration or survival of dopaminergic neurons in a subject with Parkinson's disease by administering an antagonist of NgR1, including antibodies, and including antagonists made from the soluble receptor sNgR1.

Applicants argue that the instant specification does enable a method of treating Parkinson's disease by administering antagonists of NgR1 (Remarks, p. 19). The examiner agrees that clinical efficacy of the claimed methods is not a requirement of enablement (Remarks, p. 19, second paragraph).

The examiner contends that the specification is not enabling for claims 22, 23, 35 and 36 because applicants have failed to demonstrate a nexus between Parkinson's disease and NgR1, such that administration of sNgR1 will slow or reverse the loss of cells in the substantia nigra. In addition, methods of treatment, even if performed in animals, must be sufficiently described such that undue experimentation is unnecessary. There is no data showing that the soluble NgR1 receptor is effective in treating a patient with Parkinson's disease or even an animal model of Parkinson's disease. Applicants fail to teach how to use sNgR1 to treat patients or subjects, along with guidance as to the route, duration, and quantity of administration of the disclosed sNgR1 to a subject; such information is not provided by the instant specification. The instant specification also fails to disclose how these parameters are to be determined, how a similar product was practiced in the art, or to provide even a single working example of the sNgR1 ligand being used to treat Parkinson's disease. In the absence of just such guidance, a practitioner would have to resort to a substantial amount of undue experimentation involving the compositions, variations in the amounts, the mechanics of administration deep into the brain, and the duration of

administration of the recited ligands in order to determine whether the claimed product is effective in treating Parkinson's disease.

Claim Rejections: Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and In *re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 22 and 23 *remain* provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 103 and 104 of copending Application No. 2009/0215691 (serial No. 12/335,328).

Applicants have not argued the validity of the rejection, only that it be kept in abeyance until allowable subject matter is identified (22 December 2009, p. 27).

Conclusion: Claims 1-4, 6, 10-12 and 19-36 are rejected for the reasons recited above.

THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Advisory information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sandra Wegert whose telephone number is (571) 272-0895. The examiner can normally be reached Monday - Friday from 9:00 AM to 5:00 PM (Eastern Time). If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Gary Nickol, can be reached at (571) 272-0835.

The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR

system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (in USA or CANADA) or 571-272-1000.

/SLW/
7 April 2010

/Dong Jiang/
Primary Examiner, Art Unit 1646